REMARKS

In the claims

Claims 26-28 are amended to correct antecedent basis by reciting "the chemotherapeutic agent." Claims 26-28 are also amended to clarify antecedent basis by reciting that the infection prevents "the ras-activated neoplasm from developing" drug resistance to the chemotherapeutic agent.

Claims 27 and 28 are amended to delete the phrase "wherein the reovirus is administered prior to administration of the chemotherapeutic agent" from claim 27 and the phrase "wherein the reovirus and the chemotherapeutic agent are administered concurrently" from claim 28. Support may be found, for example, in the specification at page 8, lines 25-26, which states "The reovirus may be administered any time with respect to the chemotherapeutic agent."

Claim 27 is amended to delete element (a), and elements (b) and (c) are redesignated (a) and (b). Support is provided, for example, in claim 26 as previously presented and in the specification at page 8, lines 18-23.

The preceding amendments are made to make the claims more consistent and definite, and are not intended to limit the claims in any way.

Claim 27 is amended to recite "administering, to a subject having a ras-activated neoplasm capable of developing drug resistance to a chemotherapeutic agent, an effective amount of reovirus under conditions which result in infection of the ras-activated neoplasm by the reovirus." Support is provided in the claim's recitation of "preventing a ras-activated neoplasm in a subject from developing drug resistance to a chemotherapeutic agent," because prevention of an outcome (e.g., developing drug resistance) necessarily requires that the outcome is possible (e.g., "capable of developing resistance").

Claim 28 is amended to recite "determining, in a subject having a ras-activated neoplasm, if the ras activated neoplasm includes ras-activated neoplastic cells that are refractory to a chemotherapeutic agent" as supported, for example, at page 11, lines 14-19:

> A neoplastic cell that is **"refractory" to a chemotherapeutic agent is a neoplastic cell not killed or growth inhibited** by the chemotherapeutic agent. To **determine if a**

> **neoplastic cell is growth inhibited**, the growth rate of the cell in the presence or absence of the chemotherapeutic agent can be determined by established methods in the art. The neoplastic cell is not growth inhibited by the chemotherapeutic agent if the growth rate is not significantly different with or without the chemotherapeutic agent. (Emphasis added)

New claims 52 and 53, dependent on claim 26, are directed, respectively, to administration of the reovirus prior to and concurrently with the chemotherapeutic agent. Likewise, new claims 54 and 55 are added, dependent on claim 27, and new claims 56 and 57 are added, dependent on claim 28. Support may be found, for example, in the specification at page 8, lines 26-27, which states "Preferably, the reovirus is administered prior to or concurrently with administration of the chemotherapeutic agent."

New claims 58 and 59, dependent on claims 26 and 28, are directed to ras-activated neoplastic cells that are refractory to the chemotherapeutic agent as supported, for example, at page 6, lines 20-21, which state "The cell may be susceptible to the chemotherapeutic agent in the absence of reovirus, but it is preferably refractory to the chemotherapeutic agent."

No new matter is added by the preceding amendments. Moreover, Applicants note that independent claims 26-28 are within the scope of Groups I-III as rejoined by the Examiner in the Office Action mailed May 20, 2004. The Examiner is respectfully requested to enter the preceding amendments and examine the instant claims.

New Matter Objection under 35 U.S.C. § 132

Claims 6, 8-11, 16, 26-30 and 35-51 are objected to under 35 U.S.C. § 132. The Examiner alleges that the step "(a) identifying a subject including ras-activated neoplastic cells susceptible to a chemotherapeutic agent" is new matter.

Section 706.03(o) of the M.P.E.P. states in part:

> If new matter is added only to a claim, an objection using this paragraph should not be made, but the claim should be rejected using form paragraph 7.31.01. [*"this paragraph" refers to Form Paragraph 7.28, "Objection to New Matter Added to Specification"*]

Consequently, the objection under 35 U.S.C. § 132 is improper because the alleged new matter was added to the claims, not the specification.

Further, the phrase "(a) identifying a subject including ras-activated neoplastic cells susceptible to a chemotherapeutic agent" is **not new matter**.

Section 2163.07(a) of the M.P.E.P. states:

> By disclosing in a patent application a device that inherently performs a function or has a property, operates according to a theory or has an advantage, a patent application necessarily discloses that function, theory or advantage, even though it says nothing explicit concerning it. The application may later be amended to recite the function, theory or advantage without introducing prohibited new matter. In re Reynolds, 443 F.2d 384, 170 USPQ 94 (CCPA 1971); In re Smythe, 480 F. 2d 1376, 178 USPQ 279 (CCPA 1973).

The specification teaches, for example, "a method of treating a subject with a proliferative disorder, said subject comprising neoplastic cells which are refractory to a chemotherapeutic agent" (page 7, lines 17-19). Inherent in treating a subject with a particular characteristic is a step of identifying such a subject for treatment.

Further, the specification teaches an active, independent step of determining whether a neoplastic cell is refractory to a chemotherapeutic agent or whether it is growth-inhibited (i.e., susceptible) by a chemotherapeutic agent:

> A neoplastic cell that is "refractory" to a chemotherapeutic agent is a neoplastic cell not killed or growth inhibited by the chemotherapeutic agent. To **determine if a neoplastic cell is growth inhibited**, the growth rate of the cell in the presence or absence of the chemotherapeutic agent can be determined by established methods in the art. The neoplastic cell is not growth inhibited by the chemotherapeutic agent if the growth rate is not significantly different with or without the chemotherapeutic agent. (page 11, lines 14-19, emphasis added)

Consequently, the specification supports a step of "(a) identifying a subject including ras-activated neoplastic cells susceptible to a chemotherapeutic agent."

For at least these reasons, the objection under 35 U.S.C. § 132 is improper, and Applicants respectfully request that it be withdrawn.

New Matter Rejection under 35 U.S.C. § 112, 1st Paragraph

Claims 6, 8-11, 16, 26-30 and 35-51 stand rejected under 35 U.S.C. § 112, 1st Paragraph. The Examiner alleges that the phrase "(a) identifying a subject including ras-activated neoplastic cells susceptible to a chemotherapeutic agent" is new matter.

As discussed above for the objection under 35 U.S.C. § 132, the active step "(a) identifying a subject including ras-activated neoplastic cells susceptible to a chemotherapeutic agent" is supported by the specification and therefore is **not new matter**.

Also, the Examiner infers an unwarranted limitation from Applicants' previous reply. The Examiner says that "in the response filed on Feb. 23, 2006 that the identification step of (a) in claims 26, 27 and 28 occur concurrently with the steps (b) and (c) of administering the reovirus and chemotherapeutic agent." However, the February 23, 2006 response actually states:

> In addition to the support contained in original claim 26, the specification provides additional disclosure of each step of this claim. **For example**, at page 22, lines 8-15 the specification describes preventing a neoplasm from developing drug resistance. This paragraph describes the use of reovirus to treat a subject "at the onset of the course of chemotherapy such that all cells are killed or inhibited, including drug resistant cells." Clearly a "course of chemotherapy" given to a subject where "all the cells" includes drug sensitive cells as well as drug resistant cells identifies a subject including neoplastic cells susceptible to a chemotherapeutic agent. (page 8 under "New Matter Objection and Rejection," emphasis added)

Thus, the support cited in the February 23, 2006 response is an **example.** The further support in the specification at page 11, lines 14-19, as noted in the previous section, shows that the identification step (a) in claim 26 can **also** be an independent step.

With respect to instant claim 27, identification step (a) has been deleted. For instant claim 28, step (a) has been amended as supported at page 11, lines 14-19, as noted in the previous section. Thus, the rejection is moot for these claims.

For at least these reasons, the rejection under 35 U.S.C. § 112, 1st Paragraph is improper, and Applicants respectfully request that it be withdrawn.

Rejections under Obviousness-Type Double Patenting

Claims 6, 8-11, 16, 26-30 and 36-51 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over: claims 1 and 28 of U.S. Patent No. 6,565,831B1 (the '831 patent) in view of Smith, Exp. Opin. Invest. Drugs, 2000, Vol. 9, No. 2, 311-327 (the "Smith reference") or claims 1,2-8, 13-20, 24-34 of Lee et al., U.S. Patent No. 6,136,307A (the '307 patent) in view of the Smith reference.

With respect to instant claim 26, the step of "identifying a subject including ras-activated neoplastic cells susceptible to a chemotherapeutic agent" is not taught or suggested in the claims of either the '831 patent or the '307 patent. The Smith reference does not remedy these defects.

Also, the claims of the '831 patent and the claims of the '307 patent, either alone or in combination with the Smith reference, do not teach or suggest all the limitations of claim 27. In particular, none of these references teach or suggest the step of "administering, to a subject having a ras-activated neoplasm capable of developing drug resistance to a chemotherapeutic agent, an effective amount of reovirus." In fact, none of these documents even teach or suggest drug resistance to a chemotherapeutic agent, nor how one would select a subject for treatment that has a neoplasm capable of developing drug resistance.

Further, the claims of the '831 patent and the claims of the '307 patent, either alone or in combination with the Smith reference, do not teach or suggest all the limitations of claim 28. In particular, none of these references teach or suggest the step of "determining, in a subject having a ras-activated neoplasm, if the ras activated neoplasm includes ras-activated neoplastic cells that are refractory to a chemotherapeutic agent." In fact, these documents do not even teach or suggest cells that are refractory to a chemotherapeutic agent.

With respect to instant claims 26-27, the claims of the '831 patent and the claims of the '307 patent, either alone or in combination with the Smith reference do not teach or suggest the development of drug resistance to a chemotherapeutic agent, let alone preventing a ras-activated neoplasm from developing drug resistance to a chemotherapeutic agent.

Since independent claims 26, 27 and 28 are nonobvious, the remaining rejected claims, being dependent therefrom, are also nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); MPEP 2143.03.

For at least these reasons, the instant claims are nonobvious over the claims of the '831 patent and the claims of the '307 patent, either alone or in combination with the Smith reference. Applicants respectfully request withdrawal of the corresponding rejection under the judicially created doctrine of obviousness-type double patenting.

Rejections under 35 U.S.C. § 103(a)

Claims 6, 8-11, 16, 26-30 and 36-51 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over: the '307 patent in view of the Smith reference; Lee et al., WO00/50051A2 (the '051 application) in view of the Smith reference; Mercer University Home page 1996, pp 1-2 (the "Mercer reference," www.mercer.edu/publications/discoveries/96-97/cancer.htm accessed June 18, 2004) in view of the Smith reference; and over the Smith reference alone.

With respect to instant claim 26, none of the '307 patent, the '051 application or the Mercer reference teach or suggest a step of "identifying a subject including ras-activated neoplastic cells susceptible to a chemotherapeutic agent."

Also, none of the '307 patent, the '051 application or the Mercer reference teach or suggest all the limitations of claim 27, in particular, a step of "administering, to a subject having a ras-activated neoplasm capable of developing drug resistance to a chemotherapeutic agent, an effective amount of reovirus." In fact, none of these documents even teach or suggest drug resistance of a ras-activated neoplasm to a chemotherapeutic agent, nor how one would select a subject for treatment that has a ras-activated neoplasm capable of developing drug resistance.

Further, none of the '307 patent, the '051 application or the Mercer reference teach or suggest all the limitations of claim 28, in particular, a step of "determining, in a subject having a ras-activated neoplasm, if the ras activated neoplasm includes ras-activated neoplastic cells that are refractory to a chemotherapeutic agent." In fact, these documents do not even teach or suggest ras-activated neoplastic cells that are refractory to a chemotherapeutic agent.

With respect to instant claims 26-27, none of the '307 patent, the '051 application or the Mercer reference teach or suggest preventing a ras-activated neoplasm from developing drug resistance to a chemotherapeutic agent.

Moreover, as noted in the previous section, the Smith reference does not remedy these defects.

Consequently, independent claims 26, 27 and 28 are nonobvious, and the remaining rejected claims, being dependent therefrom, are also nonobvious.

For at least these reasons, the instant claims are nonobvious over the '307 patent, the '051 application and the Mercer reference, either alone or in combination with the Smith reference, or the Smith reference alone. Applicants respectfully request withdrawal of the corresponding rejections under 35 U.S.C. § 103(a).

Rejections under 35 U.S.C. § 102(a)

Claims 6, 8-11, 16, 22, 26-28 and 36-51 stand rejected under 35 U.S.C. § 102(a) as being anticipated by the '307 patent, or alternatively, as being anticipated by the '051 application.

As noted in the previous section, neither the '307 patent nor the '051 application teach all the limitations of the independent claims, such as: a step of "identifying a subject including ras-activated neoplastic cells susceptible to a chemotherapeutic agent" as required by claim 26; a step of "administering, to a subject having a ras-activated neoplasm capable of developing drug resistance to a chemotherapeutic agent, an effective amount of reovirus" as required by claim 27; or a step of "determining, in a subject having a ras-activated neoplasm, if the ras activated neoplasm includes ras-activated neoplastic cells that are refractory to a chemotherapeutic agent" as required by claim 28. In fact, neither the '307 patent nor the '051 application teach the development of resistance to a chemotherapeutic agent, let alone the specific limitations of the instant claims.

Since independent claims 26, 27 and 28 are not anticipated, the remaining rejected claims, being dependent therefrom, are also not anticipated.

For at least these reasons, the instant claims are not anticipated by the '307 patent or the '051 application. Applicants respectfully request withdrawal of the corresponding rejections under 35 U.S.C. § 102(a).

Conclusion

For the reasons set forth above, Applicants submit that the claims of this application are patentable. Reconsideration and withdrawal of the Examiner's objections and rejections are respectfully requested. Allowance of the claims of this application at an early date is earnestly solicited.

The excess claim fees in the amount of $175.00 are being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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